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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/929,769	08/14/2001	Wei-Qiang Gao	P5007R1	9616

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EXAMINER	
RAWLINGS, STEPHEN L	
ART UNIT	**PAPER NUMBER**
1642	9

DATE MAILED: 07/14/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/929,769	GAO ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 April 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-15* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The election without traverse filed April 23, 2003 in Paper No. 8 is acknowledged and has been entered. Applicants have elected group III, claims 1-15, insofar as the claims are drawn to an antibody, or conjugate or derivative thereof, which binds a polypeptide having an amino acid sequence that is at least 80% identical to the amino acid sequence set forth in SEQ ID NO: 7.

2. In addition, Applicants' election of the species of invention in Paper No. 8 is acknowledged. However, because Applicants did not distinctly and specifically point out the errors, if any, in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Applicants have elected the species of invention wherein the cytotoxic agent conjugated to the antibody is a toxin, namely maystansinoid.

3. The amendment filed April 23, 2003 as part of Paper No. 8 is acknowledged and has been entered. Claims 1 and 2 have been amended.

4. Claims 1-15 are pending in the application. Claims 1, 7, 9, and 10, in part, have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species of invention, there being no allowable generic or linking claim.

5. Claims 1-15, insofar as the claims are drawn to an antibody, or conjugate or derivative thereof, which binds a polypeptide having an amino acid sequence that is at least 80% identical to the amino acid sequence set forth in SEQ ID NO: 7, and wherein said conjugate comprises a toxin, namely a maystansinoid or calicheamicin, are currently under prosecution.

Election/Restrictions

6. The requirement to elect a species of invention wherein said antibody of claim 1 is conjugated to maystansinoid or calicheamicin, as set forth in section 5 of the Office action mailed April 9, 2003 (Paper No. 7) has been withdrawn.

Priority

7. Applicants have not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. § 120 as follows:

The specification states that this application is a continuation of US Application No. 09/888,257, filed June 22, 2001; however, the disclosure of this application, as filed, differs from the disclosure of US Application No. 09/888,257. In particular, it is noted that the sequence set forth as SEQ ID NO: 7 in this application is not the same as the sequence set forth as SEQ ID NO: 7 of US Application No. 09/888,257; moreover, the sequence set forth as SEQ ID NO: 7 in this application does not appear to be disclosed in US Application No. 09/888,257.

To receive benefit of the earlier filing date under 35 USC §120, the later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

Additionally, Applicants' claim for priority of the earlier filing dates of the provisional US applications to which US Application 09/888,257 claims priority under 35 U.S.C. 119(e) is acknowledged. As Applicants' claim for priority of the early filing date of US Application 09/888,257 is improper, Applicants are not entitled to the earlier filing dates of the US provisional applications to which US Application 09/888,257 claims priority under 35 U.S.C. 119(e). Nevertheless, it is duly noted that US Provisional Application Nos. 60/089,653, 60/090,355, 60/104,257, 60/141,037, 60/145,698, and 60/162,506 fail to provide adequate support under 35 U.S.C. 112 for claims 1-15 of this

application, because in particular, none of these applications disclose a polypeptide having an amino acid sequence that is identical to that set forth in this application as SEQ ID NO: 7. Furthermore, although US Provisional Application No. 60/119,537 discloses a polypeptide having an amino acid sequence that is identical to that set forth in this application as SEQ ID NO: 7, this application has not been filed by an inventor or inventors named in US Provisional Application No. 60/119,537 and additionally US Provisional Application No. 60/119,537 was not pending on the date that this application was filed. Accordingly, this application is not entitled to the benefit of US Provisional Application No. 60/119,537 under 35 USC § 119(e).

Finally, with the exception of PCT/US99/28551, filed December 2, 1999, the PCT applications do not disclose a polypeptide having an amino acid sequence that is identical to that set forth in this application as SEQ ID NO: 7; and the inventor named in PCT/US99/28551 has not filed this application. Therefore, this application is not entitled to the benefit of priority under 35 USC § 365(a) to PCT/US99/28551 or any of the other PCT applications to which Applicants have claimed priority.

It is noted, however, that Applicants are entitled to claim the benefit of the filing date of PCT/US01/25464, but as this application was filed on the same date as PCT/US01/25464, the claim would not benefit the Applicants.

Accordingly, the effective filing date of this application is considered to be the date the application was filed, namely August 14, 2001.

Oath/Declaration

8. The declaration filed January 9, 2002 in Paper No. 4 is found objectionable because the declaration states that Applicants claim the benefit under 35 USC § 119(e) of US Provisional Application Nos. 60/089,653, 60/090,355, 60/60/104,257, 60/119,537, 60/141,037, 60/145,698, and 60/162,506. Of the provisional applications to which a claim of benefit has been made, only US Provisional Application No. 60/119,537 discloses the claimed invention; yet none of the inventors named in US Provisional Application No. 60/119,537 are listed as inventors in this application. Moreover, US Provisional Application No. 60/119,537 was abandoned before this application was filed.

Furthermore, the declaration is objected to because it states that Applicants claim the benefit under 35 USC § 120 of US Application No. 09/888,257, PCT/US99/12252, PCT/US99/20111, PCT/US99/28634, PCT/US99/28551, PCT/US00/00219, PCT/US00/00376, PCT/US00/04342, PCT/US00/08439, PCT/US00/13705, PCT/US00/23328, PCT/US01/06520, and PCT/US01/20118. US Application 09/888,257 does not disclose the claimed invention. Of the PCT applications to which a claim of benefit has been made, only PCT/US99/28551 discloses the claimed invention, but the joint inventor named in PCT/US99/28551 has not filed this application, and moreover none of the inventors named PCT/US99/28551 are listed as part of the inventive entity in this application.

Specification

9. The specification is objected to because the specification discloses that this application is a continuation of US Application 09/888,257 filed June 22, 2001, PCT/US99/12252 filed June 22, 2001. This application appears not to be a continuation, but rather a continuation-in-part of US Application 09/888,257, because the disclosure of this application, as originally filed, and the disclosure of US Application 09/888,257, as originally filed, are substantially different.

10. The specification is objected to because the use of numerous improperly demarcated trademarks has been noted in this application. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks. See MPEP § 608.01(v).

Examples of improperly demarcated trademarks include Adriamycin™ (page 35), American Type Culture Collection™ (pages 56, 99, and 111), Vysis™ (page 86), Physician's Desk Reference™ (page 87), Incyte™ (page 99), Gene Logic™ (pages 100 and 103), Affymetrix (page 103), GeneArray™ (page 103), Agilent™ (page 103),

Qiagen™ (pages 107, 108, and 109), GeneSpring™ (page 103), GeneExpress™ (page 103), and Lipofectin™ (page 109).

Appropriate corrections are required. Each letter of a trademark should be capitalized or otherwise the trademark should be demarcated with the appropriate symbol indicating its proprietary nature (e.g., ™, ®), and accompanied by generic terminology. Applicants may identify trademarks using the "Trademark" search engine under "USPTO Search Collections" on the Internet at http://www.uspto.gov/web/menu/search.html.

11. The specification is objected to because of the following informalities:

(a) "Adriamycin™" is misspelled at page 35.

(b) "Qiagen™" is misspelled at page 107.

Claim Objections

12. Claim 14 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 14 recites, "which induces death of a cell to which it binds", but it appears that this property of the antibody of claim 1 would be an inherent property. As such, claim 14 does not appear to further limit the subject matter of claim 1, from which claim 14 depends.

Claim Rejections - 35 USC § 112

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. The specification is objected to and claims 1-15 are rejected under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the

invention and failing to provide an enabling disclosure, because the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from a written description (e.g., the disclosure of the claimed nucleic acid molecule's polynucleotide sequence); or (3) deposited.

Claims 1-15 are drawn to an antibody that binds a polypeptide having an amino acid sequence that is at least 80% identical to an amino acid sequence encoded by the full-length coding sequence of the cDNA contained in ATCC Deposit No. 230651. However, because the polynucleotide sequence of the cDNA contained in ATCC Deposit No. 230651 is not set forth in the specification, the cDNA contained in the deposit would be required to make and use the claimed invention. As a required element, the polynucleotide sequence of the cDNA contained in ATCC Deposit No. 230651, or the deposit itself must be known and readily available to the public, or otherwise obtainable by a repeatable method set forth in the specification. If it is not so available or obtainable, a deposit containing the claimed nucleic acid molecule may satisfy the enablement requirements of 35 USC 112, first paragraph. See 37 CFR §§ 1.801-1.809.

The referral to the deposit at page 111 of the specification is insufficient assurance that all required deposits have been made and all the conditions of MPEP 608.01 (p)(c) are met.

If a deposit has been made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

In addition to the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications. Applicant's provision of these assurances would obviate this objection/rejection.

15. Claims 1-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants' specification states the present application is a continuation of US Application No. 09/888,257 filed June 22, 2001. As such the disclosure of the present application, as originally filed, should be the same as the originally filed disclosure of US Application No. 09/888,257. However, as noted above, the disclosure of the present application and US Application No. 09/888,257 are not the same. In particular, it is noted that the sequence set forth as SEQ ID NO: 7 in this application is not the same as the sequence set forth as SEQ ID NO: 7 of US Application No. 09/888,257; moreover, the sequence set forth as SEQ ID NO: 7 in this application does not appear to be disclosed in US Application No. 09/888,257. Accordingly, the recitation of the polynucleotide sequence set forth as SEQ ID NO: 7, which is depicted in Figure 7, appears to introduce new matter, since SEQ ID NO: 7 is not disclosed in US Application No. 09/888,25, and thereby violates the written description requirement set forth under 35 USC § 112, first paragraph. Similarly, the recitation of the polynucleotide sequence encoding the amino acid sequence of SEQ ID NO: 7 in Figure 3 and in the sequence listing as SEQ ID NO: 3 appears to introduce new matter.

Amending the specification to state that this application is a continuation-in-part of US Application No. 09/888,257 could obviate this ground of rejection.

Claim Rejections - 35 USC § 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (f) he did not himself invent the subject matter sought to be patented.

17. Claims 1-9 and 13-15 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 00/36102 A2 (22 June 2000).

WO 00/36102 A2 teaches an isolated antibody that binds to a polypeptide comprising an amino acid sequence having at least 80% identity to the amino acid sequence set forth in SEQ ID NO: 7, or which binds to a polypeptide comprising an amino acid sequence that is at least 80% identical to an amino acid sequence encoded by the cDNA deposited under ATCC Deposit No. 230651. Additionally, WO 00/36102 A2 teaches that the antibody can be intact or an engineered fragment, chimeric or humanized, monoclonal or polyclonal, and/or conjugated to a growth inhibitory agent, namely a cytotoxic agent, namely a toxin. WO 00/36102 A2 teaches the antibody can be used to treat cancer. WO 00/36102 A2 teaches that once isolated a DNA molecule encoding the antibody can be placed in a vector, which can then be transfected into host cells, namely CHO cells to produce the antibody. Furthermore, WO 00/36102 A2 teaches the antibody can be detectably labeled.

18. Claims 1-9 and 13-15 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter.

The subject matter of claims 1-9 and 13-15 is disclosed in US Provisional Application No. 60/119,537 filed February 10, 1999 by Colin K. Watanabe and William I. Wood, who are not listed as inventors in the present application. Accordingly, it appears the Applicants did not invention the claimed subject matter. See MPEP § 2137.

Claim Rejections - 35 USC § 103

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

20. Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/36102 A2 (22 June 2000) in view of Fernandez et al. (*Appl Environ Microbiol* 2000 Nov; **66** (11): 5024-9) and/or US Patent No. 5,208,020 A (04 May 1993).

WO 00/36102 A2 teaches that which is set forth in the 35 USC § 102(b) rejection above.

However, while WO 00/36102 A2 teaches that an antibody can be produced in a host cell, WO 00/36102 A2 does not explicitly disclose that the host cell can be a bacterial cell. In addition, while WO 00/36102 A2 teaches that the antibody can be conjugated to a toxin and used to treat cancer, WO 00/36102 A2 does not explicitly disclose that the antibody can be conjugated to maystansinoid.

Nevertheless, WO 00/36102 A2 teaches that a protein, such as an antibody, can be produced in bacteria. Furthermore, the methods for producing recombinant proteins, including antibodies, in *E. coli* or other bacterial cells were both conventional and routine at the time the invention was made, it would have been *prima facie* obvious to one of ordinary skill in the art to produce the antibody in bacteria cells.

Even so, Fernandez et al. teaches that a simple method for the production of a recombinant antibody in bacterial cells, namely *E. coli*. Fernandez et al. teaches that the culture medium containing the antibody can be used in a variety of immunoassays without need of further purifying the antibody. Additionally, Fernandez et al. teaches that the culture medium containing the antibody can be stored for long periods without loss of activity.

Accordingly, in view of the teachings of Fernandez et al., it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have produced a recombinant antibody or antigen-binding fragment thereof, as taught by WO 00/36102 A2, in bacterial cells, such as *E. coli*, because Fernandez et al. teach a simple method for the production of a recombinant antibody in bacterial cells, namely *E. coli*. One of ordinary skill in the art at the time the invention was made would have been motivated to do so, because Fernandez et al. teaches that the culture medium containing the antibody can be used in a variety of immunoassays without need of further purifying the antibody.

Furthermore, US Patent No. 5,208,020 A teaches a cytotoxic agent comprising one or more maystansinoids linked to a monoclonal antibody or a fragment thereof, a pharmaceutical composition comprising said cytotoxic agent, and a method for treating cancer comprising administering to a subject said pharmaceutical composition, wherein the antibody or fragment thereof is selective for tumor cell antigens.

Accordingly, in view of the teachings of US Patent No. 5,208,020 A, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have produced a cytotoxic agent comprising a recombinant antibody or antigen-binding fragment thereof, as taught by WO 00/36102 A2, linked to one or more maystansinoids, because US Patent No. 5,208,020 A teaches such a cytotoxic agent, wherein the antibody or fragment thereof is selective for tumor cell antigens, can be used to treat cancer and WO 00/36102 A2 teaches that such an immunoconjugate comprising an antibody that binds specifically to a polypeptide comprising an amino acid sequence having at least 80% identity to the amino acid sequence set forth in SEQ ID NO: 7, or which binds to a polypeptide comprising an amino acid sequence that is at least 80% identical to an amino acid sequence encoded by the cDNA deposited under ATCC Deposit No. 230651, can be used to treat cancer. One of ordinary skill in the art at the time the invention was made would have been motivated to do so in order to treat cancer in a patient.

Conclusion

21. No claims are allowed.

22. The prior art made of record and not relied upon is considered pertinent to Applicants' disclosure. Zaworski et al. teaches that recombinant proteins can be produced in CHO cells in serum-free medium, which Zaworski et al. discloses provides a better system from which to purify proteins. Page et al. teaches that a humanized antibody can be successfully produced in CHO cells. Trail et al. teaches an effective means of treating cancer using an immunoconjugate comprising doxorubicin. Blakey et al. teaches an antibody-directed enzyme prodrug. Chari et al. (1992) teaches immunoconjugates comprising maystansinoids. WO 00/53750 A1 teaches compositions and methods for treatment of tumors; and in particular, WO 00/53750 A1 teaches an antibody that binds specifically to a polypeptide having the amino acid sequence set forth in SEQ ID NO: 7. US Patent Nos. 5,712,374 A and 5,877,296 A teach conjugates comprising an antibody and a calicheamicin derivative. Tolcher et al. teaches a maytansinoid immunoconjugate. Ross et al. teach prostate stem cell antigen as a therapy target. Allen et al. reviews targeted alpha therapy for cancers. Bross et al. and Knoll et al. teach immunoconjugates comprising a derivative of calicheamicin. GENBANK Accession Nos. AB037861 and BC004286 teach proteins that are similar to the polypeptide of SEQ ID NO: 7.

23. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (703) 305-3008. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C. Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1642

STEPHEN RAWLINGS

slr
July 8, 2003